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Focal Epithelial Hyperplasia (Heck's Disease) – Case Report of a Rare Disease in an Adult Caucasian Man

Choroba Hecka – opis przypadku rzadkiej choroby u dorosłego mężczyzny

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of article

Abstract

Focal epithelial hyperplasia (or Heck's disease) is an infection of the oral mucosa caused by human papillomavirus. The condition is extremely rare, with the highest incidence in tribal communities from remote Greenland, and North and South America. Only few cases have been noted in adult Caucasian patients. This paper reports on a case of focal epithelial hyperplasia in a 56-year-old man admitted to the Department of Maxillofacial Surgery, Wrocław Medical University for investigation of multiple mucosal lesions in the oral cavity. The lesions were excised under local anesthesia without any complications. According to the findings of a histopathological examination, the lesions were classed as focal epithelial hyperplasia. The diagnosis was supported by the detection of human papillomavirus subtype 32.

Physicians, dentists and other oral medicine specialists should be aware of this kind of lesions and a careful clinical observation combined with histopathological testing should be carried out to establish a definitive diagnosis (**Dent. Med. Probl. 2015, 52, 4, 516–520**).

Key words: human papillomavirus, focal epithelial hyperplasia, Heck's disease.

Słowa kluczowe: wirus brodawczaka ludzkiego, ogniskowy przerost nabłonka, choroba Hecka.

Focal epithelial hyperplasia (FEH) is also named as Heck's disease, multifocal epithelial hyperplasia, verrucae of the oral cavity or multifocal papillomavirus epithelial hyperplasia. The disease was first outlined by March in 1881 [1] and later by Stern [2] and Helms [3]. The earliest English publication was a series of 19 pediatric patients (native children from the United States and Brazil and one Eskimo child from Alaska) with intraoral papules described as focal epithelial hyperplasia by Archard et al. [4]. In 1965, Heck wrote about multiple papules spread in the oral mucosa of an 11-year-old native American girl [4, 5]. In 1966, Hettwer and Rodgers [6] named the condition "Heck's disease" in a case report of focal epithelial hyperplasia in a Polynesian girl.

The name of "focal (or multifocal) epithelial hyperplasia" seems to be the most appropriate as it reflects the main features of the disease: the presence of multiple lesions in the oral mucosa and microscopically detectable hyperplasia of the epithelium [3]. In Caucasians there have only been a few cases reported [7, 8]. A high incidence of the condition correlates with patients' communal way of living [8].

FEH usually occurs in patients aged 3–18 and is more common among females. The disease tends to spontaneously regress. However, it can also persist for many years. [9, 10]. It is characterized by the occurrence of multiple or single small papules or nodules in the oral cavity, ranging in diameter from 0.1 cm to 1.0 cm and usually coalesc-

ing [11–13]. The color of the lesions varies from red through grey to white. The lesions are usually painless, unless traumatized, and are found especially on the labial and buccal mucosa, lower lip and tongue [4].

FEH results from the subtype 13 or 32 of human papillomavirus (HPV). While the subtype 13 of HPV appears to be involved in the development of the disease in both pediatric and adult patients, the subtype 32 of HPV usually causes the disease in older age groups [8, 14–16].

The possible differential diagnoses are *condyloma acuminatum*, florid oral *papillomatosis*, Crohn's disease, Darier disease, Cowden's syndrome, focal dermal hypoplasia (Goltz syndrome) or white sponge naevus [12, 15, 16].

FEH distinct histopathological features are: epithelial hyperplasia, acanthosis and parakeratosis. Thickening and focal elevations of the epithelium may extend in an upward direction without involvement of the underlying dermis. The appearance of epithelial hyperplasia varies, including basal epithelial battle-axe-shaped projections that occasionally anastomose horizontally, koilocytes (characterized by a clear cytoplasm and absent nucleus) and other intracellular changes characteristic of viral infections such as hyperchromatism and enlargement of nuclei [17]. The degenerating epithelial cells' nuclei resemble various phases of mitosis and are called mitosoid figures [12, 18]. These are mostly found in the upper part of the epithelium and in lesions which are not fully developed but are not consistently present. There is little inflammatory infiltrate with dilated capillaries and some lymphocytes in the connective tissue [19]. Dyskeratosis, binucleation, exocytosis and basal vacuolation have occasionally been observed [20].

Case Report

A 56-year-old Caucasian man was referred to the Department of Maxillofacial Surgery, Wrocław Medical University for examination and treatment of multiple mucosal lesions in the oral cavity. The patient was otherwise medically fit and his physical examination showed no significant abnormalities. None of his blood relatives have been diagnosed with similar lesions.

An intraoral examination revealed several exophytic, sessile, smooth-surfaced nodules situated on the lingual surface of the lower lip (10 × 40 mm) and the right (9 × 36 mm) and the left (14 × 18 mm) lateral surfaces of the tongue (Fig. 1–3). The lesions were firm on palpation, ranged from 1 to 4 mm in diameter, and were cov-



Fig. 1. FEH mucosal changes situated on the lingual surface of the lower lip



Fig. 2. Multiple lesions of FEH on the right lateral surface of the tongue



Fig. 3. FEH lesions on the left lateral surface of the tongue

ered with a normal whitish-pink mucosa that was neither inflamed nor ulcerated. There were no other oral or extraoral lesions. The lesions were

noticed 1 year ago by a dentist and were asymptomatic. They never interfered with mastication. Prior to hospitalization, the patient had not travelled abroad for two years.

Due to the rare clinical presentation and concerns of the patient, excisional biopsies of the lesion areas were performed under local anesthesia (2% lignocaine HCl with 1:100,000 adrenaline) without any complications. Postoperatively, the wound has healed well.

The biopsy specimens were fixed in 10% formaldehyde and sent off for histological examina-

tion. Microscopically, the hematoxylin and eosin-stained sections of these 3 specimens were very similar and showed a squamous epithelium with focal hyperkeratosis, parakeratosis, acanthosis, verrucous proliferation and papillomatosis, hyperplasia of basal cells, isolated perinuclear cellular vacuolization (koilocytosis) and cellular binucleation (Fig. 4, 5). There were some well-isolated mitosoid cells too. Furthermore, the presence of a mild squamous dysplasia area with a diameter of 1 mm was identified in the specimen from the right lateral border of the tongue.

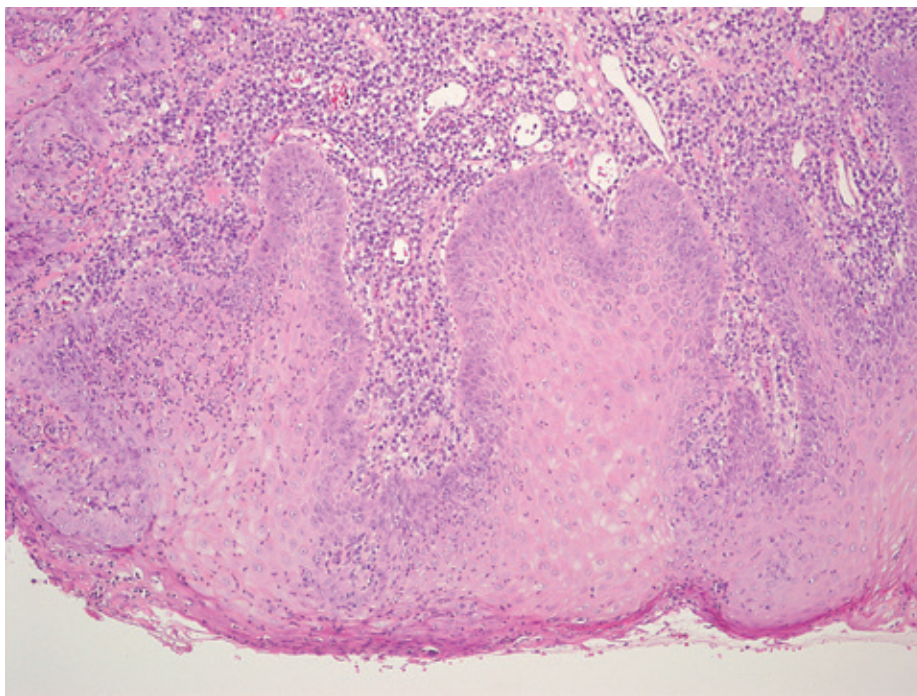


Fig. 4. Parakeratosis and acanthosis of squamous epithelium (hematoxylin-eosin, 100×)

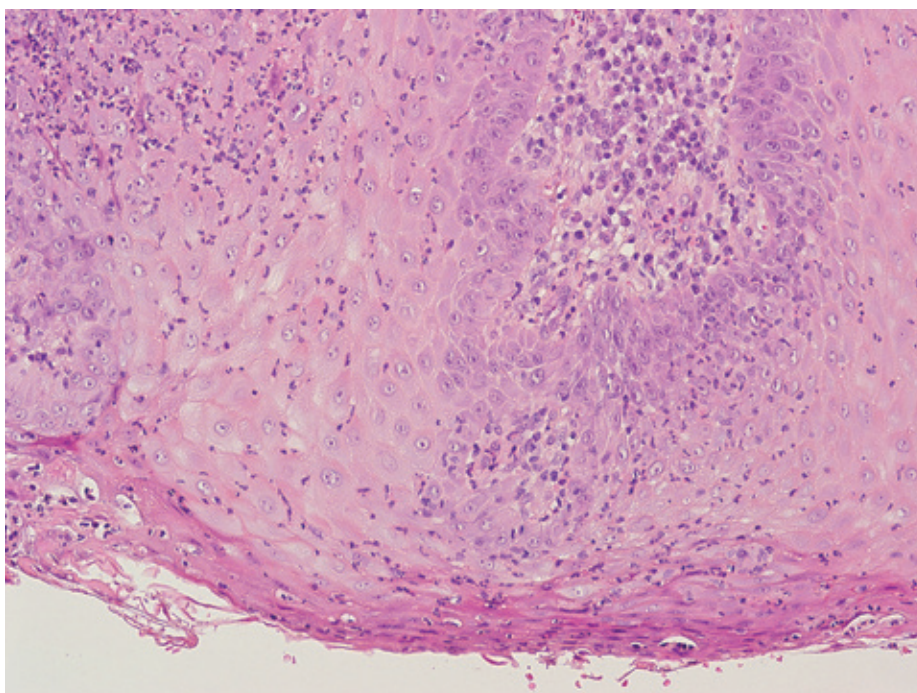


Fig. 5. Nuclear changes produced by human papillomavirus in focal epithelial hyperplasia (hematoxylin-eosin, 200×)

The clinical and histological features were typical of FEH. A PCR analysis was carried out to confirm the diagnosis, and HPV-32 was clearly detected in DNA samples extracted from the lesion.

Because of the benign nature of the disease, no further treatment was needed and this was explained to the patient. The patient was followed up for 6 months, with no signs of reoccurrence noticed.

Discussion

Although FEH is predominantly encountered in remote populations in America [5], it has also been reported in other geographical regions. Rare cases of FEH in Caucasian patients have been noted, with the disease occurring mostly in older adolescents and adults.

The etiopathogenesis of FEH is not fully known. An infectious character of the disease is supported by a high incidence among family members and in secluded communities [20–23]. A viral etiology has been evidenced by several immunocytochemical and *in situ* hybridization studies that have identified the presence of human papillomavirus (HPV) subtypes 13 and 32. Human papillomavirus subtypes 1, 6, 11 and 55 have also been implicated [3, 12, 24–28]. It has been postulated that an infection with these viruses leads to irreversible cellular degeneration and affects the expression of cytokines 14, 15, 16 and 19, which is thought to result in an alteration in cytokeratin immune reactivity and may modify the metabolic pattern of epithelial cytokeratins [3].

Host factors such as genetic predisposition, immune suppression, malnutrition and insufficient hygiene are important etiological factors [10], and a combination of these factors seems to increase an

individual's risk of FEH [3]. The genetic predisposition has been suggested based on multiple reports of the disease occurring in various familial ethnic groups such as native communities from North and South America as well as in Inuit from Greenland [5, 29], as it may make an individual's immune system susceptible to acquiring certain types of HPV infection [28]. An association between HLA-DR4 (DRBI*0404) and HPV infections has been discovered lately in a Mestizo population from Mexico [26]. Recent studies on FEH indicate a relationship with stated chronic immunodeficiency. FEH is rarely associated with detectable immune suppression. However, increased incidence of FEH in HIV-positive patients has been observed [18, 29, 30]. It is suggested that the immunodeficiency in HIV infection increases the risk of the HPV-related FEH and its subsequent recurrences, but the relationship needs further studies. The relationship between a mechanical factor such as fixed metal-ceramic prosthesis and FEH has also been suggested [31].

Due to the benign clinical course of FEH and its association with minimal carcinogenic HPV serotypes, no aggressive therapy is usually recommended [10]. Surgical removal of the lesions is advised to patients with aesthetic concerns or interference with occlusion. Therapeutic options for the treatment of FEH include surgical excision, cryosurgery, carbon dioxide and diode laser removal, injections or topical application of interferon β or podophyllin, topical and systemic retinoids and vitamins [17].

Reports on the presence of FEH in specific geographical areas and in HIV-infected patients should alert all clinicians to the possible occurrence of the disease. The aim of this report is to educate and inform oral medicine specialists so that they will be able to recognize, diagnose and manage focal epithelial hyperplasia correctly.

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